

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph bridging pages 5 and 6 with the following amended paragraph:

Figure 3 is divided in three panels: Panel A shows the restriction maps in kilobases (kb) and the distribution of the genes in the operon *apxI* from the genome of App. In light gray, the *apxIA* gene is depicted, being the target of the different recombination events, and in dark gray the adjacent genes *apxIC*, *apxIB* and *apxID*. The different genes or regions of plasmid pApxIΔH2 are drawn using skewed bars. The coding fragments of the transmembrane helices (H1, H2 and H3) of ~~apxIA~~—*apxIA* are highlighted in Black. The names and some detailed structures in figure 2 plasmids have been simplified. Thus gfpUV comprises the ptac promoter and the atpE/GFPUV fusion; OriV indicates the vegetative origin of replication of R6K and OriT the origin of transference by conjugation of RP4. In (1) and (3) both are shown the restriction map obtained with enzyme *XhoI* and the distribution of the genes of operon *ApxI* of the App genome are shown. In (2) the restriction map of the same operon after the insertion of plasmid pApxIΔH2 in the App genome is shown. This insertion occurs by a unique homologous recombination event between flanking regions 5' of H2 placed in plasmid pApxIΔH2 and the App genome respectively.

Please replace the paragraph bridging pages 6 and 7 with the following amended paragraph:

Figure 4 is divided in 3 panels: Panel A shows the restriction maps (in kb) and the distribution of the genes in operon *apxII* located in the App genome. In light grey the *apxIIA* gene is depicted. This is the target of the different recombination events. The adjacent genes *apxIIC*, *apxIIB* are depicted in dark grey; The different genes or regions of plasmid pApxIIΔH2 are drawn using skewed bars. The coding fragments of the transmembrane helices (H1, H2 and H3) of ~~apxIIA~~—*apxIIA* are highlighted in black. The restriction map obtained

with the enzyme *EcoRI* and the distribution of the *ApxII* operon genes of the *App* genome are shown in (1) and (3). The restriction map of the same operon after the insertion of *pApxIIΔH2* plasmid in (2) is depicted. This insertion is done through a unique homologous recombination event between the 3' flanking regions of *H2* located in plasmid *pApxIIΔH2* and the *App* genome. In (4) the restriction map of the operon is depicted after the resolution of the plasmid inserted in (2) after a second recombination through the 5' flanking regions of *H2* located in the *App* genome.

Please replace the fourth paragraph (lines 15-20) on page 11, with the following amended paragraph:

C.2 . Construction of a hybrid cloning vector which contains the 5' and 3' flanking sequences of the second transmembrane helix, specified by the ~~*apxIA*~~-*apxIA* gene. Therefore, the hybrid plasmid *pApxIΔH2* was constructed in order to select and clone such fragments adjacent to the 5' and 3' ends of the segment that codes the second transmembrane helix in the *apxIA* gene. This plasmid was used as the final vector for the transformation of *App*.

Please replace the paragraph bridging pages 24 and 25 with the following amended paragraph:

E.- Analysis of the DNA purified from the colonies, isolated in the previous passage, to test the homogeneity of the cultures and the presence of the deletion in genes ~~*apxIA*~~-*apxIA* and *apxIIA*.

Please replace lines 2-14 on page 15 of the specification, with the following:

The techniques and DNA recombinant methods applied as follows, are described in detail in Sambrook and Russell (In Molecular cloning 3rd Ed. Cold Spring Harbor Laboratory Press, Cold spring Harbor New York (2001) and Ausubel et al; *Current Protocols in Molecular Biology*, John Wiley and Sons, Inc. (1998)). All PCR products were previously cloned in a pBE plasmid before being digested with restriction enzymes. This plasmid is a derivative of pBluescript SK2 (~~Stratagene~~STRATAGENETM) vector and presents the multiple cloning site substituted by a small nucleotidic sequence which specifies only the target of the restriction enzyme *EcoRV*.

The *E. coli* XL1-blue strain (~~Stratagene~~STRATAGENETM) has been used as a host for hybrid vectors based on plasmids pUC118 or pBluescript SK. The *E. coli* S17-1 λ pir strain (Simon et al; Biotechnology 1:784-791 (1983)) has been used as a host of the hybrid vectors based in plasmid pGP704.

Please replace the heading E.1. on page 25 (line 8), with the following:

E.1.- Analysis of the ~~apx/IIH2~~apx/IIH2⁻ recombinants.

Please replace the heading E.2. on page 26 (line 27), with the following:

E.2.- Analysis of the ~~apx/IIIH2~~apx/IIIH2⁻ recombinants.